

Immunization

Providing immunity by artificial means

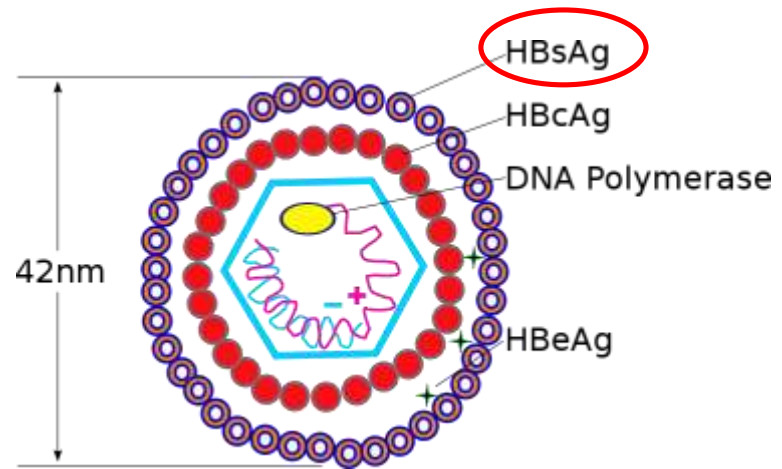
Mohammed Asaad El-Mowafy

Main points of the lecture:

- **A story of vaccine development using HBV as an example.**
- **Passive and active immunity.**
- **Types of vaccine and Antiserum**
- **Common ingredients in vaccines**
- **Storage, transport and administration of vaccines**
- **Routine immunization against infectious diseases**

A story of vaccine development !! , HBV

The hepatitis B virus was discovered in 1965 by Dr. Baruch Blumberg who won the Nobel Prize (in 1976) for his discovery.



Electron microscope

Format: Abstract

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N Engl J Med. 1975 Nov 20;293(21):1063-7.

Hepatitis B "immune" globulin: effectiveness in prevention of dialysis-associated hepatitis.

Prince AM, Szmunes W, Mann MK, Vyas GN, Grady GF, Shapiro FL, Suki WN, Friedman EA, Stenzel KH.

Abstract

A randomized, double-blind, multicenter study of hepatitis prevention by immune serum globulin with high anti-HBs titer ("hepatitis B immune globulin") was carried out among 318 new patients and 296 staff members of renal dialysis units. Three milliliters of high titer globulin, repeated at four months, was compared with equal doses of intermediate or normal titer globulin. Among staff members, the cumulative percentages developing hepatitis or HBs Ag, or both, within eight months were 6.9, 11.7, and 11.1 in the high, intermediate, and normal titer groups respectively. The lower incidence associated with high titer globulin was not significant (P greater than 0.05). However, among the patients the respective percentages were 7.9, 21.3, and 23.1 and the lower incidence in the high titer globulin group was significant.

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Efficacy of a heat inactivated hepatitis B vaccine in male homosexuals: outcome of a placebo controlled double blind trial.

[R A Coutinho](#), [N Lelie](#), [P Albrecht-Van Lent](#), [E E Reerink-Brongers](#), [L Stoutjesdijk](#), [P Dees](#), [J Nivard](#), [J Huisman](#), and [H W Reesink](#)

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This article has been [cited by](#) systematic reviews in PubMed.

Abstract

The efficacy of a heat inactivated hepatitis B virus vaccine, containing 3 micrograms hepatitis B surface antigen (HBsAg), was studied in a high risk group of 800 susceptible homosexual men by a randomised placebo controlled double blind trial. At the trial end point (21.5 months), 17 hepatitis B virus infections had occurred in vaccinated subjects (attack rate 4.8%) and 56 in subjects receiving a placebo (attack rate 23.8%). This reduction in the incidence of hepatitis B virus infections in vaccinated subjects was highly significant (p less than 0.0001). Two months after the first injection 72.3% of the vaccinated subjects had formed antibodies against hepatitis B surface antigen, and this percentage increased to 89% at four months. Maximum anti-HBs titres were reached five months after the first vaccination, the geometric mean titre being 107.6 mIU. Even vaccinated subjects with a low antibody response (greater than or equal to 1 and less than 10 mIU) were found to be protected from HBsAg positive infections. The vaccine had no serious side

HBsAg vaccine produced by recombinant protein technology:

- Prepared by production of recombinant protein expression in *Saccharomyces cerevisiae*.
- Approved to be used in human in 1991.
- E.g. Engerix B (Glaxo)



Passive immunity:

- Antibodies from another person or animal are injected or transfused into an individual who receives “passive” immunity.
- This form of immunization has the advantage of providing immediate protection, it is effective for a short duration only.
- 1- Naturally acquired passive immunity:

Immunity is transferred from mother to fetus through placental transfer of IgG or colostral transfer of IgA.
- 2- Artificially acquired passive immunity:

Passive immunity:

2- Artificially acquired passive immunity:

- ❑ Immunity is often artificially transferred by injection with immunoglobulin from other individuals or from an immune animal (antiserum).
- ❑ Passive transfer of immunity with immune globulin is practiced in numerous acute infections (diphtheria, tetanus, measles, rabies, etc.), poisoning (insect-, reptile-bites, botulism), and as a prophylactic measure.

Active immunity:

This refers to immunity produced by the body following exposure to antigens.

1- Naturally acquired active immunity:

Exposure to different pathogens leads to clinical infections, which normally result in a protective immune response against these pathogens.

2- Artificially acquired active immunity:

Immunization may be achieved by administering live or dead pathogens or their components (Vaccination).

Vaccine:

- **It is a special preparation of antigenic material that can be used to stimulate the development of antibodies and thus confers artificial active immunity against specific disease or number of diseases.**
- **Vaccination is often carried in a two or three stages as separate doses.**
- **Booster dose: Additional dose of a vaccine to maintain a lifelong immunization.**
- **A vaccine is usually given by injection, and for some diseases, oral vaccines are also available.**

Vaccine:

According to preparation : It is prepared either as stock or autogenic vaccine:

- **Stock vaccine: Prepared from standard laboratory strains.**
- **Autogenic vaccine: prepared from infecting strain (from patient).**

Examples of abbreviations of vaccines:

Pathogen	Vaccine Abbreviation
Bacterial	
<i>Mycobacterium Tuberculosis</i>	BCG
Diphtheria, Tetanus, & Pertussis	DTP
<i>Haemophilus influenzae type b</i>	Hib
Viral	
Hepatitis A	HepA
Hepatitis B	HepB
Measles, Mumps, Rubella	MMR
Measles, Mumps, Rubella, Varicella	MMRV

- It should be mentioned that the abbreviation of a virus differs from brand name or the trade name e.g. one of the brand names of HepB is Engerix-B
- BCG comes from Bacillus Calmette-Guérin strain

Types of vaccine :

- **A- Live attenuated vaccines**
- **B- Killed vaccines**
- **C- Subunit vaccines**

A- Live attenuated vaccines:

- **It is the reduction of the disease producing ability (virulence) of bacteria or virus under laboratory conditions.**
- **These pathogens will grow in the vaccinated individual, but because they are weak, they will cause no disease.**
- **Vaccination by these weakened organisms will produce a limited infection and the immune system of normal healthy people quickly kill and eliminate them from the body with production of antibodies which give the immunity to the persons.**

A- Live attenuated vaccines:

- **Because these vaccines replicate, the immune response is long-lasting, mostly lifelong.**
- **Examples of live vaccines: measles, mumps, and chicken pox (varicella) are used routinely.**
- **In the case of viruses or intracellular microorganisms, where cell-mediated is usually desired, attenuated pathogens are capable of replicating within host cells.**

A- Live attenuated vaccines:

➤ Advantages:

- 1- Stimulate an excellent continual immune response that is nearly as good as compared to an infection with the wild-type pathogen.
- 2- A single dose produces long lasting immunity which reinforced by booster doses.

➤ Examples :

Bacterial live attenuated vaccine: BCG

Viral live attenuated vaccine: Measles, Oral polio vaccine (OPV), and Rotavirus.

A- Live attenuated vaccines:

➤ Disadvantages:

1- They carry a serious risk of causing disease in immunocompromised individuals (postvaccine complications).

2- Since live vaccines are often attenuated (made less pathogenic) by passage in animal or thermal mutation, they can revert to their pathogenic form and cause serious illness.

**** For this reason, polio live vaccine, which was used for many years, has been replaced in many countries by the inactivated vaccine.**

➤ As a precaution, live attenuated vaccine tend not to be administered during pregnancy.

B- Killed vaccines:

- **These consist of whole organisms inactivated by heat, chemicals or UV irradiation treatment.**
- **Some of these are used to immunize people at risks (e.g. influenza, hepatitis A) while others are used to immunize travelers to different countries (e.g. cholera, typhoid).**
- **Advantage: They can be used for immunocompromised patient.**
- **Disadvantage: Several doses are required to produce complete immunization, usually three successive doses, 4-6 weeks in between and booster doses are necessary.**

C- Subunit vaccines:

- Subunit vaccines contain purified products that usually come from the bacteria or virus that causes natural infection, but may also be synthesized in the laboratory using recombinant technology.
- They are inactivated bacterial toxins (toxoid), or polysaccharide material or proteins components or purified viral antigen such as HBsAg which stimulate the body to produce immune response.
- Such as:
 - *Tetanus* and *Diphtheria* (inactivated exotoxin)
 - *Haemophilus influenza* b, *Neisseria meningitidis* polysaccharides
 - Hepatitis B (surface antigen-recombinant antigen vaccine)

Antiserum:

- **Plueral : Antisera**
- **A serum that contains antibodies against antigens of a particular kind.**
- **It may be injected to treat or to give temporary protection against certain disease.**
- **Antisera are prepared in large quantities in animals.**
- **In the laboratory they could be also used to identify unknown organisms responsible for infection.**
- **E.g.: Botulinum antitoxin produced in Equine (horses) , It is used in the treatment of Botulism (strong food poisoning) as the antitoxin neutralize the free toxins.**

Common ingredients in vaccines:

➤ Adjuvants

➤ Preservatives

➤ Others:

- Antibiotics
- Sugars, amino acids, and proteins.
- Monosodium glutamate and 2-phenoxy-ethanol
- Formaldehyde
- Fetal (calf) bovine serum

Adjuvants:

➤ **Definition:**

Any substance used in conjunction with another to enhance its activity.

Or

A substance added to a vaccine to enhance the immune response by intensity and/or duration.

- **There are many biological and chemical substances that have been used in experimental conditions.**
- **Mainly Aluminum salts aluminum hydroxide, and aluminum salts e.g. aluminum phosphate, alum (potassium aluminum sulfate), or mixed aluminum salts are often uses as adjuvants.**

Preservatives:

- **Preservatives are added to some vaccine formulations to prevent the growth of bacteria or fungi that may be introduced into the vaccine during its use, e.g., repeated puncture of a multi-dose vaccine vial with a needle.**
- **E.g. Thiomersal that is a mercury-containing preservative that is added to vials of vaccine that contain more than one dose.**

Antibiotics, sugars, amino acids, and proteins:

➤ Antibiotics:

- **Mainly neomycin, polymyxin B, streptomycin and gentamicin.**
- **Used in some production methods for making inactivated influenza virus vaccines.**
- **The very small amounts of antibiotics contained in vaccines have not been clearly associated with severe allergic reactions.**

Antibiotics, sugars, amino acids, and proteins:

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➤ Sugars, amino acids, and proteins:

Sugars e.g. sucrose and lactose, amino acids such as glycine proteins such as human serum albumin or gelatin are stabilizers for lyophilized vaccines.

- **Monosodium glutamate and 2-phenoxy-ethanol which are used as stabilizers in a few vaccines to help the vaccine remain unchanged when the vaccine is exposed to heat, light, acidity, or humidity.**

Formaldehyde & Fetal (calf) bovine serum :

➤ Formaldehyde:

- **Used to inactivate viruses so that they don't cause disease (e.g., polio virus used to make polio vaccine) and to detoxify bacterial toxins, such as the toxin used to make diphtheria vaccine.**
- **Formaldehyde is diluted during the vaccine manufacturing process, and the amount of formaldehyde present in some vaccines are not considered to cause safety problems.**

➤ Fetal (calf) bovine serum:

Present in some viral vaccines, when the virus is grown in cell lines. (From the preparation of vaccines against some viruses)

Transport , and storage of vaccines:

- **Vaccines must be stored at temperature 2 to 8 ° C from the place of manufacture to the point of administration.**
- **So a careful cold system should be used for transporting vaccines.**
- **Vaccines must not be freezed or subjected to high temperature.**

Adminstration of vaccines:

- **Most vaccines are given to children because they are more subjected to diseases.**
- **Each country has its childhood immunization schedule, which determines the time of child vaccination and the time of the booster doses required for some vaccines.**
- **Travelers to endemic areas, vaccination against typhoid, cholera, yellow fever and meningitis.**
- **Health care team immunization against TB and hepatitis B.**
- **Vaccination against influenza for elder patients, chronic respiratory diseases and immunocompromized patients.**

Routine immunization against infectious diseases:

➤ 1- Poliomyelitis:

There are two types of vaccines:

- IPV killed polio vaccine is available (IM injection).**
- OPV, sabine vaccine, oral polio vaccine (live attenuated) is widely used.**

➤ Disadvantages of live attenuated polio vaccine

1- Rarely reversion of the attenuated virus to virulence will occur and cause disease.

2- It can not be given to immunocompromised person or pregnant woman because the fetus may become infected.

➤ Schedule of vaccination:

- 6 doses of OPV at 0, 2, 4 and 6, 9, 12 months. Each dose is 2 drops in mouth.**
- Booster doses are recommended 18 months.**

Routine immunization against infectious diseases:

➤ 2- MMR:

- **It is live attenuated vaccine against measles, mumps and rubella.**
- **It is given to children of 12 (1st dose), 18 (2nd) month age and non immunized adults.**
- **A third dose is given to 4-6 years children.**
- **Fever and rash for 1-2 days are rarely occurring.**

➤ 3- BCG (Tuberculosis):

- **Live attenuated vaccine BCG (Bacillus Calmette- Guerin) is required.**
- **It is given intradermally to neonate 2-4 weeks (or at birth) and unimmunized adults 10 – 14 years**
- **Adverse side effect: local abscesses.**

Routine immunization against infectious diseases:

➤ 4- DTP immunization :

- It is the vaccination against Diphtheria, Pertussis and tetanus.
- It consists of toxoids diphtheria and tetanus and pertussis (sub-unit vaccine).
- The primary course of the triple vaccine is administered as three doses at 2, 4, 6 months of age.

➤ 5- Hib (Haemophilus influenzae b):

- The infection with *Haemophilus influenzae b* occurs in children before 4 years (the major cause of bacterial meningitis).
- It can now be administered with DTP vaccine.

Routine immunization against infectious diseases:

➤ 6- Hepatitis B:

- Three doses are recommended at intervals of 2, 4, and 6 months (IM injection).**
- It is also recommended for people exposed to blood or blood products, healthcare team and patient receiving much transfusion or dialysis**

Routine immunization against infectious diseases:

➤ 7- Immunization of specific risk group:

a) Meningococcal :

- MenC vaccines are available for group A and group C of *Neisseria meningitides*.
- Recommended for contact with infected persons and travellers to endemic area.

b) Hepatitis A: It is recommended for travellers to endemic area.

c) Cholera: It is recommended for travellers to endemic area. It provide protection 3- 6 months.

d) Influenza:

- Influenza vaccine is regularly updated due to the development of new virulent strains.
- Protection lasts for one year.

Basic vaccine schedule in Egypt:

التحسينات الإجبارية			
ملاحظات	اسم القائم بالتطعيم والوحدة	تاريخ التطعيم	التطعيم ضد الأمراض
			ضد الدرن: شلال الخمسة عشر يوماً الأولى من الولادة ضد شلل الأطفال: جرعة صفوية: خلال الأسبوع الأول من الولادة. جرعة أولى: عند إتمام شهرين من العمر ... جرعة ثانية: عند إتمام ٤ شهور من العمر ... جرعة ثالثة: عند إتمام ٦ شهور من العمر ... جرعة رابعة: عند إتمام ٩ أشهر من العمر ... جرعة خامسة: عند إتمام ١٢ شهراً من العمر ... جرعة متشعبة: عند إتمام ١٨ شهراً من العمر ... ضد الدفتريا والتيتانوس والسعال الديكي: جرعة أولى: عند إتمام شهرين من العمر ... جرعة ثانية: عند إتمام ٤ شهور من العمر ... جرعة ثالثة: عند إتمام ٦ شهور من العمر ... جرعة متشعبة: عند إتمام ١٨ شهراً من العمر ... ضد الالتهاب الكبدي (ب): جرعة أولى: عند إتمام شهرين من العمر ... جرعة ثانية: عند إتمام ٤ شهور من العمر ... جرعة ثالثة: عند إتمام ٦ شهور من العمر ... ضد الحصبة والحصبة الألمانية والنكاف: جرعة أولى: عند إتمام ١٢ شهراً من العمر ... جرعة ثانية: عند إتمام ١٨ شهراً من العمر ...
			تحسينات أخرى: ١- ... ٢- ... ٣- ... ٤- ... ٥- ...

إرشادات

يادر بتطعيم طفلك ضد الأمراض المعدية بالجرعات المقررة في المواعيد المحددة،

- ١- التطعيم ضد الدرن يقي طفلك من مرض خطير يستمر علاجه سنين عديدة.
- ٢- التحصين ضد شلل الأطفال يقي طفلك من مرض يسبب عجزاً أو عاهات قد تستمر طوال الحياة.
- ٣- التطعيم بالطعم الثلاثي البكتيري يقي طفلك من ثلاثة أمراض خطيرة (الدفتريا - التيتانوس - السعال الديكي).
- ٤- التطعيم ضد الالتهاب الكبدي (بي) يقي طفلك من مرض الالتهاب الكبدي (بي) الخطير.
- ٥- التطعيم بالطعم الثلاثي الفيروسي يقي طفلك من أمراض: (الحصبة - الحصبة الألمانية - النكاف).

Basic vaccine schedule in Egypt:

العمر	الجرعة	الطعم	المرض	الكيفية
عند الميلاد	الجرعة المصيرية	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان
	جرعة واحدة	بي سي جي	التطعيم ضد الدرن	حقناً في الجلد بالكف الأيسر
شهران	الجرعة الأولى	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان بالفم
		الخماسي	التطعيم ضد الدفتريا والسعال الديكي والتهانوس والكبد (ب) والإنتانزا البكتيرية	حقناً بالعضل بالخذ الأيسر
4 شهور	الجرعة الثانية	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان بالفم
		الخماسي	التطعيم ضد الدفتريا والسعال الديكي والتهانوس والكبد (ب) والإنتانزا البكتيرية	حقناً بالعضل بالخذ الأيسر
6 شهور	الجرعة الثالثة	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان بالفم
		الخماسي	التطعيم ضد الدفتريا والسعال الديكي والتهانوس والكبد (ب) والإنتانزا البكتيرية	حقناً بالعضل بالخذ الأيسر
9 شهور	الجرعة الرابعة	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان بالفم
		فيتامين (أ)		على اللسان بالفم
12 شهر	الجرعة الخامسة	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان بالفم
		إم. إم. أر	التطعيم ضد الحصبة والنكاف والحصبة الألمانية	حقناً تحت الجلد بالذراع الأيمن
18 شهراً	جرعة منشطة	سايبرين	التطعيم ضد شلل الأطفال	نقطتان على اللسان بالفم
		التلاتي	التطعيم ضد الدفتريا والسعال الديكي والتهانوس	حقناً بالعضل بالخذ الأيسر
		إم. إم. أر	التطعيم ضد الحصبة والنكاف والحصبة الألمانية	حقناً تحت الجلد بالذراع الأيمن
		فيتامين (أ)		على اللسان بالفم

Thanks for your attention

Questions 